INFORMATION FOR
HEALTH PROFESSIONALS

Data Sheet

HAEMACCEL®

Polygeline

Presentation

HAEMACCEL is manufactured from gelatin derived from BSE-free bovine material sourced only from the USA. HAEMACCEL is a clear, sterile, pyrogen free, ready for use solution which contains no preservatives.

Uses

Actions

Pharmacological properties

Physico-chemical Data:

	Haemaccel 3.5%	Albumin 5%
Mean Molecular weight (Dalton)	approx. 30 000	66 000
Relative viscosity (35°C)	1.7 - 1.8	1.9 - 2.3
Dynamic viscosity	cP 1.15 - 1.20	1.12
Isoelectric point	pH 4.7 (± 0.3)	4.9 (± 0.2)
pH of infusion solution	7.3 ± 0.3	7.2 ± 0.1
Colloid-osmotic (oncotic) pressure (37°C)	3.4 - 3.8 kPa	3.2 - 3.4 kPa
Osmolality	293 mOsm/kg	
Osmolarity	301 mOsm/l	

Haemaccel is pharmacologically inert.

1. Effect on extracellular fluid volume: Following intravenous administration, Haemaccel is distributed between intravascular and extravascular compartments. Fluid is not drawn from the extravascular compartment and the increase in intravascular volume will never exceed the volume of Haemaccel infused. The higher molecular weight fractions are retained in the intravascular compartment and excreted more slowly. In surgical patients with varying degrees of blood loss and renal efficiency, the intravascular half life of Haemaccel has been established to be 4-6 hours.

2. Effect on Renal Function: Increases in glomerular filtration rate and renal plasma flow, as well as a decrease in renal vascular resistance, have been observed after Haemaccel.

Patients in shock demonstrate a marked increase in diuresis after Haemaccel infusion. No effect on serum sodium and potassium levels has been observed, despite an increase in excretion of the electrolytes.

3. Effect on coagulation and fibrinolysis: Haemaccel in large or repeated doses has not exhibited any interference with haemostatic mechanisms in vivo.

4. Effect on blood-grouping, cross-matching and blood sedimentation rate: There is no evidence that Haemaccel infusions are likely to interfere with blood-typing or cross-matching, even if fast tests are used.

Pharmacokinetics

Absorption: Haemaccel is administered by intravenous infusion.

Metabolism: In vitro, it has been demonstrated that gelatin and Haemaccel-polygeline similarly, are broken down into small

peptides and amino acids by proteolytic enzymes such as trypsin, plasmin or cathepsin. It is assumed that the same processes apply in vivo.

Distribution and Excretion: Following intravenous infusion of 500 mL Haemaccel the intravascular distribution is completed after a few circulatory passages and followed by an elimination phase with a half-life of approximately 8 hours. The apparent volume of distribution is 8 L (12 L/100 kg body wt). Excretion proceeds at a non dose-dependent rate and the main route of excretion is renal (80%). Intestinal excretion and metabolic breakdown do also occur to a smaller extent.

The elimination half-life from the blood appears to vary according to different investigators from 5 hours to 8 hours.

Increase in intravascular volume immediately after infusion will be of the order of 350 mL or 500 mL following the administration of 500 mL or 1000 mL of Haemaccel respectively.

The elimination half-life is increased by age, and by the presence of severely impaired renal function. The excretion is rather slower in patients with blood loss than in normal volunteers.

Two hours after the infusion of 500 mL Haemaccel around 30% has been excreted, after 24 hours 49-59%, and after 48 hours 50% or 47-65% depending on the study. Accumulation does not occur.

Two hours after administration of labelled polygeline approximately 3% has been traced in the form of CO_2 in expired air, indicating metabolism.

Indications

1. Prevention or treatment of shock associated with reduction in effective circulating blood volume due to:
   a. Haemorrhage (visible, concealed).
   b. Loss of plasma (burns, peritonitis, pancreatitis, crush injuries).
   c. Loss of water and electrolytes from persistent vomiting and diarrhea.
2. As a plasma substitute in surgery where controlled haemodilution is employed.
3. Procedures involving extra-corporeal circulation e.g. filling the heart-lung machine.
4. Carrier for insulin infusion
5. Isolated organ perfusion

In addition HAEMACCEL can be used as a vehicle for various medicines.

Dosage and Administration

Haemaccel is administered intravenously, and can be infused immediately.

Adults -

1. Prevention or treatment of shock associated with reduction in effective circulating blood volume due to:

(i) Haemorrhage

Blood loss up to 1500 mL - correct by use of Haemaccel alone.

Blood loss in the range 1500-4000 mL - recommended ratio Haemaccel/whole blood is 1:1

Blood losses above 4000 mL - recommended ratio Haemaccel/whole blood is 1:2.

The rate of infusion and total dose employed will be governed by clinical assessment. In acute situations of severe rapid blood loss, large volumes and rapid infusion may be required. The haematocrit should not be permitted to fall below 25 to 30% volume during therapy.

(ii) Relative hypovolaemia

Normovolaemia and a high speed of Haemaccel infusion are considered as factors contributing to anaphylactoid reactions in susceptible individuals.

Where Haemaccel is used to restore circulating blood volume in the absence of loss of intravascular fluid, the patient should be carefully observed for skin reactions, difficulty in breathing or precipitous fall in blood pressure.

(iii) Burns.

The management of extensive burns should be undertaken by specialized units. The volume of Haemaccel and crystalloid given should be varied according to the clinical response of the patient and the assessment of renal function.

(iv) Water and electrolytes

Haemaccel may be used to restore deficiencies in circulating blood volume in conditions such as persistent vomiting and diarrhoea.

2. As a plasma substitute in controlled haemodilution

Haemaccel has been employed in autologous blood transfusion and haemodilution techniques involving the collection of two or three units of patient's blood just prior to surgery; 2-3 units of blood are withdrawn from patients after the induction of anaesthesia for major vascular surgery, each unit being simultaneously replaced by 500 mL of Haemaccel. During the operation, blood losses are immediately replaced with an equal volume of Haemaccel, as long as the haematocrit is above 0.25-0.30, or with blood alone when the haematocrit falls below this level.

3. Procedures involving extracorporeal circulation, e.g. for filling the heart-lung machine

Silvay et al. (1968) recorded very favourable results using a mixture of heparin stabilised whole blood and Haemaccel for filling the pump oxygenator used in conjunction with cardiac surgery in a series of 45 patients. 500-2000 mL of Haemaccel were used in each instance. Merikallio (1976) used a Haemaccel/physiological saline/bicarbonate solution to prime the heart/lung machine for 40 patients undergoing cardiac surgery with cardio-pulmonary bypass. 1000 mL of Haemaccel were used for each operation.

Ibister (1977) lists Haemaccel as possible fluid replacement for patients undergoing plasmapheresis. The infusion rate used varies from 20-80 mL/min depending on haematocrit, viscosity and total extracorporeal pumping volume per minute.

Stellon and Moorhead (1981) used Haemaccel alone as a replacement fluid in several patients undergoing plasma exchange involving the removal of 2.5 litres of plasma. They concluded from their observations of total protein, albumin and globulin, that for patients on weekly plasma exchange no plasma proteins fractions need to be administered. Hamilton et al (1980) recorded the use of the plasma protein fraction/Haemaccel/physiological saline for plasma exchange in patients with SLE.

Paediatric. - As for Adult above.

Geriatric. - As for Adult above.

With impaired hepatic function. - No modification necessary.

With impaired renal function. Haemaccel has a beneficial effect on renal function and no exacerbation of pre-existing renal disease need be expected.

Note that in the case of babies, infants and elderly persons such patients have inadequate reserves of protein.

Administration

Haemaccel is to be infused intravenously. The speed and duration of the infusion depends on the needs of the individual patient.

The infusion speed is to be adjusted in accordance with the monitored blood pressure values. The drip rate can be calculated using the following formula:

e.g. 500 mL to be infused in 1 hour.

$$\frac{500}{4 \times 1\ (h)} = 125 \text{ drips per minute}$$

In emergencies it is possible to administer Haemaccel as a rapid infusion (e.g. 500 mL in 6 to 15 min.)

Contraindications

Known hypersensitivity to constituents of Haemaccel.

Existing anaphylactic/ anaphylactoid reactions.

Warnings and Precautions

Haemaccel has been associated with rare but severe reactions similar to anaphylaxis. Patients should be monitored carefully for relevant symptoms and signs so that product infusion can be stopped and appropriate urgent treatment commenced.

Rapid infusion of Haemaccel may stimulate release of histamine. Urticaria and rarely bronchospasm and hypotension may occur. (See **ADVERSE EFFECTS**).

Administration of red cell concentrate or whole blood is required where blood losses exceed 25% of the blood volume or when haematocrit falls below 25% by volume.

In the presence of cardiac insufficiency, hypertension, cardiogenic shock, pulmonary oedema, oesophageal varices, haemorrhagic diathesis or anuria, the infusion of Haemaccel should be made only with proper controls because haemodilution or an increase in intravascular/interstitial fluid volume may be hazardous in these conditions. Blood losses up to 25% of the blood volume can be replaced by Haemaccel alone.

Care should be taken when Haemaccel is given to patients with known allergic conditions such as asthma, to patients with a history of histamine response or to patients who have received a histamine releasing drug (See **INTERACTIONS**) within 7 days prior to Haemaccel administration, as these patients are probably at an increased risk of histamine release. In such cases, Haemaccel may be given only after the prophylactic use of H_1 and H_2 receptor antagonists.

The infusion of Haemaccel may result in a temporary increase in the erythrocyte sedimentation rate.

Due to the calcium content of Haemaccel, the serum calcium concentrations may be found to be slightly elevated for a temporary period, especially when large amounts of Haemaccel are administered by rapid infusion.

Care should be taken if large amounts of Haemaccel are infused as haemodilution can lead to decreased coagulation potential.

Infuse clear solutions only. Once the bottle is opened, the solution should be used immediately. Any unused contents should be discarded, since Haemaccel contains no preservative.

For technical reasons there is a residual air volume in the container. Thus, pressure infusions with the plastic infusion bottle must be carried out under controlled conditions only, as the risk of an air embolism cannot be excluded

Use in Pregnancy and Lactation

Haemaccel, for its usual indications, is not contra-indicated in pregnancy. However, particular care should be exercised when fluid or volume replacements are administered during or immediately after pregnancy.

It is not known whether polygeline is excreted in breast milk. Haemaccel is employed during and following labour and no harmful effects on the newborn have been reported.

Adverse Effects

During or after the infusion of any volume-expanding solution, there may be side-effects of varying intensity. Transient skin reactions (urticaria, wheals), hypotension, tachycardia, bradycardia, nausea/vomiting, dyspnoea, rises in temperature and/or chills may occasionally occur.

However, rare cases of anaphylactoid reactions have been reported, with bronchospasm, tachycardia, severe hypotension and life-threatening shock. Angioedema oedema has also been reported in such instances.

These side effects seem more likely to occur when Haemaccel is infused rapidly into patients with normovolaemia. These reactions are due to histamine release and may be the result of the cumulative effect of histamine-releasing drugs (See **INTERACTIONS**). They are not true anaphylactic reactions on an immunological basis. If side-effects occur, the infusion should be discontinued immediately. If necessary, treatment should be given as follows:

Management of Anaphylactic and Anaphylactoid Reactions:

Mild Reactions:

Administer corticosteroids and antihistamines.

Severe Reactions:

1. Cease administration of Haemaccel Immediately
2. Administer oxygen by face mask at 6-8L/min.
3. a) Adults - inject adrenaline 1:1000 IM
   small adults (<50kg) 0.25mL
   average adults (50 - 100kg) 0.50mL
   large adults (>100kg) 0.75mL
   b) Children (to age 12)
   Use adrenaline 1:10 000 Or Dilute 1 ampoule (1mL) of adrenaline 1:1000 with 9mL water for injection or normal saline inject intramuscularly 0.25mL per year of age (approximates to 5 mg/kg)
4. Establish one, or preferably two, wide bore intravenous lines (16 gauge or larger). Commence rapid fluid resuscitation with normal saline, etc.
5. If there is severe laryngospasm, bronchospasm, circulatory shock or coma, intubate the trachea and commence intermittent positive pressure ventilation.
6. If there has been little or no response to the initial intramuscular dose of adrenaline, administer the same dose slowly into the intravenous line. Repeat at 5 minute intervals depending on response. If the patient remains shocked, start an adrenaline infusion (preferably via a central venous line), commencing at 0.25 mg/kg/min and titrating as required to restore blood pressure. Large doses of adrenaline may be needed.

Interactions

Citrated (conserved) blood should not be mixed with Haemaccel or transfused immediately before or after Haemaccel using the same venous access, since the Ca^{++} content of citrated blood will cause recalcification. However, citrated blood can be transfused into a separate venous access from that of Haemaccel. Haemaccel and heparinized blood can be mixed freely.

A decrease in blood pressure caused by the cumulative effects of histamine releasing drugs (anaesthetics, muscle relaxants, analgesics, ganglia blockers, and anticholinergics) is not an indication for rapid infusion of Haemaccel.

If cardiac glycosides are being given simultaneously, attention must be paid to the synergistic effect of calcium in Haemaccel.

Overdosage

Haemaccel does not lead to a substance specific impairment of coagulation or platelet function. However, if large amounts of Haemaccel are given, the circulatory parameters should be monitored closely. A possible haemodiluting effect might act on the coagulation potential and on the corpuscular parts of the blood.

Pharmaceutical Precautions

Provided sterile precautions are observed, Haemaccel may be mixed with ordinary infusion fluids (saline, glucose, Ringer's solution, etc.) and with the drugs acting on the cardiovascular system, corticosteroids, muscle relaxants, barbiturates, vitamins, streptokinase and antibiotics of the penicillin series and cefotaxime, provided they are water-soluble.

Citrated blood (stored blood for transfusion) must not be mixed with Haemaccel (because the calcium ions in Haemaccel would cause recalcification). However, it may be transfused into a separate venous access from that of the infusion of Haemaccel. There is no objection to mixing heparinized blood with Haemaccel. In common with all infusion fluids, Haemaccel - for physiological reasons - should not be administered at low temperatures.

The infusion of Haemaccel may result in a temporary increase in erythrocyte sedimentation rate.

Medicine Classification

Pharmacy-Only Medicine

Package Quantities

Haemaccel is available in flexible plastic infusion bottles each containing 500 mL of a 3.5% colloidal solution of polygeline.

Further Information

List of exipients

		mmol/L	g/L
Cations:	Na^+	145	3.33
	K^+	5.1	0.20
	Ca^{++}	6.25	0.25
Anions:	Cl^-	145	5.14

Traces of PO_4^{3-} and SO_4^{2-}; in addition, anionic polypeptides up to the isoionic point.

Water for Injections. B.P. up to 1000mL

Haemaccel is sterile and pyrogen free, and contains no preservatives

Storage and Shelf Life

Recommended storage is between +2°C to +25°C and shelf-life, five years from date of manufacture.

If Haemaccel is stored at above +25°C the stated expiry date has to be reduced by 2 years.

As proved by viscosity measurements freezing and thawing does not cause any change in the physico-chemical properties. The infusion solution must not be used after the expiry date given on the pack and container. Once an infusion bottle has been opened, any unused contents are to be discarded.

Instructions for Use and Handling

The use of disposable infusion devices is recommended to avoid transmission of pyrogen substances.

For physiological reasons Haemaccel should not be infused in the cold state, like all infusion solutions.

Infuse clear solutions only.

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